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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,846	01/13/2000	DAVID A. ESTELL	GC381-US	5580

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EXAMINER

STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 10/17/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/462,846

Applicant(s)

ESTELL, DAVID A.

Examiner

David J. Steadman

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 30 September 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☐ The period for reply expires ___ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) ☐ they raise the issue of new matter (see Note below);
 - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: see attached.

3. ☐ Applicant's reply has overcome the following rejection(s): see attached.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☐ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 1,4-9 and 13-21.

Claim(s) withdrawn from consideration: 2,3 and 10-12.

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s): _____.
10. ☐ Other: _____

ADVISORY ACTION

1. Claims 1-21 are pending in the application.
2. Claims 2, 3, and 10-12 remain withdrawn from consideration.
3. Claims 1, 4-9, and 13-21 stand finally rejected.
4. No claim is in condition for allowance.
5. The request for reconsideration in the after final amendment of Paper No. 17, filed 09/30/02, is acknowledged. While the amendment to the claims would appear to overcome claim objections and rejections under 35 USC 112, first and second paragraphs, the amendment does not place the claims in condition for allowance because the amendment would require further consideration of the claims and a new rejection under 35 USC 112, second paragraph. See MPEP 714.13 regarding non-entry of after final amendments.
6. Specifically, claim 6 would require a new rejection under 35 USC 112, second paragraph as lacking antecedent basis. Claim 6 recites the limitation "[t]he microorganism" in claim 1. There is insufficient antecedent basis for this limitation in the claim.
7. In view of applicants' comments regarding the use of the term "wpr" (see page 4 of Paper No. 17), the objection of claims 15, 17, and 21 for the use of the term "wpr" is withdrawn.
8. The objection to claim 13 for grammatical and spelling errors is maintained. The after final amendment to the claim as set forth in Paper No. 17 would appear to overcome the objection, however, in view of the non-entry of the amendment, the rejection is maintained for the reasons of record.
9. The rejection of claims 20 and 21 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "*Bacillus* comprises the nucleic acid sequence set forth in SEQ ID NO:1" is maintained. The after final amendment to claim 20 as set forth in Paper No. 17 would appear to overcome the rejection, however, in view of the non-entry of the amendment, the rejection is maintained for the reasons of record.
10. The written description rejection of claims 16-19 under 35 U.S.C. 112, first paragraph, is maintained. Cancellation of claims 16-19 as set forth in Paper No. 17 would overcome the rejection,

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however, in view of the non-entry of the amendment, the rejection is maintained for the reasons of record.

11. The scope of enablement rejection of claims 1, 4-9, and 13-21 under 35 U.S.C. 112, first paragraph, is maintained. The after final amendment as set forth in Paper No. 17 would appear to overcome the rejection of all claims *except* claims 13-15, 20, and 21, however, in view of the non-entry of the amendment, the rejection is maintained for all of claims 1, 4-9, and 13-21 for the reasons of record. Regarding claims 13 (claims 14 and 20 dependent therefrom), 15, and 21, undue experimentation would be required for a skilled artisan to practice the claimed invention. The claims are so broad as to encompass a method of producing a heterologous protein using a *Bacillus* host cell containing *any* mutation in the gene encoding SEQ ID NO:2 (claim 13) or SEQ ID NO:1 (claim 20) and optionally wherein the *Bacillus* host cell comprises *any* mutation in the genes encoding the proteases of claim 15 or 21. Applicants argue that *any* mutation that results in the inactivation of CP1 proteolytic activity alone or in combination with mutations in the recited proteases of claims 15 and 21 are intended. Applicants argue that they are not required to provide all mutations that result in CP1 inactivation. Applicants argue guidance has been provided in the specification as to means of identifying the presence of CP1 as well as means to assess protease activity. Applicants' argument has been fully considered but is not found persuasive. As written, claim 13 does not limit the result of the mutation of SEQ ID NO:1 or a gene encoding SEQ ID NO:2 to inactivating CP1 protease activity. As such, the specification does not provide guidance for obtaining those host cells that exhibit *any* biological activity. The specification provides guidance only for obtaining those host cells with inactivated CP1 protease activity. Regarding claims 15 or 21, the specification provides no guidance for mutating the recited proteases to obtain a desired biological activity, i.e., the mutation can result in any of the recited proteases having *any* function. It is well known in the art that the effect(s) of mutations to an encoding nucleic acid are highly unpredictable. Such mutations may result in an inactivated protein, a protein with increased activity, a protein with altered substrate specificity, and/or a protein with an entirely different function. The specification provides no guidance for mutating SEQ ID NO:1, a gene encoding SEQ ID NO:2, or the proteases of

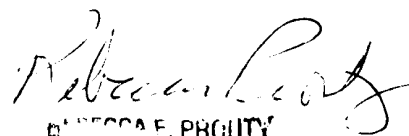
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claims 15 and 21 to obtain a protease having any function. Therefore, it would require an undue amount of experimentation to make the claimed invention.

12. Upon reconsideration of the rejection of claims 1, 4-9, and 13-21 under 35 U.S.C. 102(b) as being anticipated by WO89/10976, the rejection is withdrawn. It is noted that the reference of WO89/10976 does not disclose the sequence of the cysteine protease that was inactivated. *B. subtilis* comprises numerous cysteine proteases and there are no distinguishing features of the cysteine protease of WO89/10976 that would indicate that this protease is the same as the cysteine protease of the instant application. Therefore, it is only a possibility that the *B. subtilis* with an inactivated cysteine protease of WO89/10976 is the same as that of the claimed invention. Therefore, the rejection is withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The examiner can normally be reached Monday-Thursday from 6:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652


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